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RESEARCH ARTICLE

Comparative Study between Epidural Analgesia, Intrathecal Analgesia and Intravenous Remifentanil Analgesia in Management of Labor Pain

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Abstract

Background: Epidural analgesia is considered to be the standard method of labor analgesia, however the intrathecal (spinal) analgesia provides rapid onset with smaller doses of drugs and the intravenous remifentanil is the easiest method with rapid onset and offset. **Aim of the study:** To compare the analgesic efficacy, side effects and maternal satisfaction in these three methods. **Method:** A sample of 75 full term pregnant women at labor were recruited for this clinical trial , during the period from April 2017 to March 2018 at AL Basra General Hospital .They precluded into 3 equal groups each with 25 parturients . **Epidural group:** parturients received continuous epidural infusion with a combination of bupivacaine 0.1%and fentanyl 2µg/ml at rate of 10-15 ml/hour. **Intrathecal (spinal) group:** parturients received intrathecal (spinal) single-dose of a combination of bupivacaine 2.5 mg and fentanyl 25 µg. **Intravenous remifentanil group:** parturients received (continuous) intravenous infusion of remifentanil 0.05—0.07 µg/kg/min and a bolus (20-60 µg) doses were given during the peak of uterine contraction . Data collected were; Labor pain intensity measured by numerical rating scale (NRS) 0-10. NRS>3 was considered as failure of analgesia, maternal vital signs, with SPO2 and level of consciousness were observed every 15 minutes (in first hour) then every 30 minutes till delivery. Fetal heart rates were observed by continuous cardiotocography machine. **Results:** There were no significant differences between the characters of parturients in the three groups. Epidural analgesia provided the leas pain scores during the first stage of labor with means of NRS 1.8 ± I.5.The mean time onset of analgesia was 11±3.3 minutes in the epidural group, 5.2±1minutes in the spinal group, and 2.7± 0.7 minutes in the remifentanil group. During the second stage of labor the means of NRS were the least in the spinal 2±1. Remifentanil group showed complications like , SPO2 < 92 %(room air breathing) in 20/25 patients (80%), decrease of respiratory rate below 12 breath/minutes in 4/25 (16%) and over sedation with Ramsay score >3 in 5/25 (20%). Maternal satisfaction was higher in epidural and spinal groups than remifentanil group. **Conclusion:** The most effective analgesia during the first stage of labor was the epidural, while in the second stage was the spinal analgesia. However maternal respiratory complications were significantly more in the remifentanil group. Maternal satisfaction was higher in both epidural and spinal than the intravenous remifentanil.

Keywords: epidural _ intrathecal _ IV remifentanil _ labor analgesia.

1 | INTRODUCTION

Analgesia refers to the relief of pain without the loss of consciousness. Modalities of analgesia during childbirth include regional analgesia, systemic opioid analgesia, continuous labor support, pudendal blocks, immersion in water during the first stage of labor, sterile water injections in the lumbosacral spine, hypnosis, and acupuncture (1-8). Since 2000, regional analgesia has become the most widely used analgesia for labor pain in the United States (9). Regional analgesia leads to reversible loss of pain over an affected area by blocking the afferent conduction of its innervations with a local anesthetic agent. Epidural and spinal analgesia are two types of regional analgesia used to diminish labor pain. Epidural analgesia is recommended in labor as the 'most flexible, effective and least depressing to the central nervous system' of the choices available, according to the guidelines of the American Society of Anesthesiologists and the American College of Obstetricians and Gynecologists (10). With epidural analgesia, an indwelling catheter is directed into the epidural space, and the patient receives a continuous infusion or multiple injections of local anesthetic. Unlike epidural injections, spinal injections usually are single injections into the intrathecal space. The epidural potential space is relatively large and requires more anesthetic volume than a spinal injection. The onset of action of spinal analgesia is almost instantaneous, and one dose of medication can provide pain relief for several hours. Conversely, epidural analgesia requires at least 15 minutes until the patient's perception of pain is diminished. Spinal injections need to be placed below L1-L2; otherwise the spinal cord can be injured. Also, traditional spinal injections are more likely to affect motor as well as sensory fibers, which can limit the woman's participation in the second stage of labor (9). Several drugs have been used to initiate the spinal component of analgesia. Large doses of lipid soluble opioids produce rapid and profound analgesia but are associated with significant side effects (11– 16). Because of the synergistic effect of combining local anesthetics, the dose of opioids required to provide effective labor analgesia can be significantly reduced (17,18). Indeed, some investigations have shown that reducing the dose of spinal medications diminishes the duration of analgesia but does not affect the quality of pain relief. An intrathecal injection of a smaller combined dose of bupivacaine and fentanyl would provide rapid and effective labor analgesia in a clinically relevant population (11, 17, 19 –21). Regional analgesia in laboring patients increases the risk of vacuum or forceps assisted vaginal delivery (4). Some physicians try to reduce this risk by discontinuing epidural analgesia late in the second stage of labor. However, a meta-analysis found no statistical reduction in instrumental vaginal deliveries with this method (4). The effect of epidural analgesia on long-term neonatal outcome needs further study but appears to be safer than the use of opioids (4, 11). Systemic opioid analgesia is a commonly used adjunct with subsequent initiation of regional analgesia or an independent method of pain control used early in the first stage of labor. However, repeated maternal administration of opioids results in considerable fetal exposure and increases the potential for neonatal respiratory depression. Patient-controlled analgesia with synthetic opioids such as fentanyl, alfentanil, and the new ultra-short–acting remifentanil may be used for labor analgesia (18). The use of remifentanil for labor analgesia has grown since 1988, from a few carefully selected cases (22) to being available in over a third of units in the UK (23). Remifentanil has a substantial body of evidence that supports its use for labor analgesia; it is an ultra-short acting opioid that is rapidly and efficiently metabolized by both mother and fetus (25). A recent meta-analysis confirms that it is a more effective labor analgesic than other parenteral and inhalational alternatives (26).

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County population. Murang'a and Muriranjas are in Kiharu which has 105195, Maragua in Murang'a South 170,318, Kirwara in Gatanga has 186986. Kigumo, Kandara and Kangema have 138,432, 175,229, and 86,112 Some hospitals have developed remifentanil analgesia either for women with contraindications to regional analgesia or where an 'epidural on demand' service is not provided (23).

Aim of the study: To compare the analgesic efficacy, side effects and maternal satisfaction in these three methods: epidural, spinal and intravenous remifentanil in management of labor pain.

2 | MATERIALS AND METHOD

After obtaining approval of hospital ethics committee and parturients informed consents, a sample of 75 full term pregnant women during labor were recruited for this clinical trial, during the period from April 2017 to March 2018 at AL Basra General Hospital .The inclusion criteria were; gestational age of ≥ 36 weeks, normal cephalic presentation and cervical dilatation ≥ 5 cm .They precluded into 3 equal groups each with 25parturients

Epidural group: An epidural catheter was placed under aseptic technique at the L3-L4 or L4-L5 interspaces. A test dose of 3 ml of 2 % lidocaine was administered, and epidural analgesia was established with initial bolus of 10 ml bupivacaine 0.1 % plus fentanyl 2.5 µg/ml. Analgesia was maintained by continuous infusion by syringe pump machine (TOP-5300) of bupivacaine 0.1 % plus fentanyl 2.5 µg/ml at a rate of 10-15 ml/hour aiming to obtain sensory block to T-10 level (27). Intrathecal (spinal) group: Under aseptic technique; a single injection of the lumbar spines with Quincke spinal needle gauge 25G at the L3-L4 or L4-L5 interspaces was done. A dose of 2.5 mg hyperbaric bupivacaine 0.5 % (0.5ml) plus fentanyl 25µg (0.5 ml), a total volume of one ml (31).

Remifentanil group: An intravenous cannula was cited for remifentanil delivery. The remifentanil concentration used was 20 µg/ml (1 mg diluted to 50 ml of normal saline). A loading bolus of 0.5 µg/kg was infused over 20 seconds, and after a 5 minutes another bolus of 0.25 µg/kg. Followed by continuous infusion by syringe pump machine (TOP-5300) of 0.05-0.07 µg/kg/min and intermittent boluses 20-60 µg were given on demand (during the peak of uterine contraction) (34).

3 | MONITORING

1. Maternal heart rates, noninvasive blood pressure monitoring, SPO2, respiratory rates and electrocardiography.
2. The level of sensory block was checked bilaterally 5 cm from the midline by ice cube (28).
3. Maternal sedation was assessed by: Ramsay score;

1= anxious, agitated or restless,

2= cooperative, oriented and tranquil,

3= responsive to commands only,

4= brisk response to light glabellar tap,

5= sluggish response to light glabellar tap,

6= no response (24).

4. Maternal satisfaction scoring:

1= not satisfied,

2= satisfied,

3= very satisfied (29).

5. Fetal heart rates were observed by: Cardiotocograhy machine.

4 | RESULTS

The baseline Characteristics of the groups were comparable as shown in (Table -1) bellow.

Table 1: *Characteristics of the groups (Mean ±SD)*

Variables	Epidural group n=25	Spinal group n=25	Remifentanil group n=25	P-value
Age (year)	25±6	26±6	23±6	0.237
Body mass index	28±3	28±5	28±3	0.687
Gestation (week)	436±	436±	436±	
Cervical dilatation (cm)	5.3±0.8	6.5±0.8	6±1	0.001
Parity	1.4±1.4	1.8±2	1±1.4	0.333
Mean blood pressure (mmHg)	92±7	91±7	87±10	0.101
Heart rates (beat/min)	95±10	98±10	92±14	0.189
Respiratory rates (cycle/min)	19±1	19±1	19±1	0.942
SPO_2 %	98±0.5	98±0.5	98±0.5	0.829
Fetal heart rates (beat/min)	140±3	139±3	138±3	0.050

There were no significant differences in intensities of labor pain between the groups before interventions, however epidural group showed the least pain intensity during the first stage of labor with NRS mean 1.8±1.5 followed by 3.9±1 for spinal and 4.9±1 for remifentanil (P< 0.01).During delivery spinal group presented the least pain intensity with NRS mean 2±1 ,followed by 3.5±1 for epidural and 6±1 for remifentanil (P< 0.01) as shown in table-2.Time onset of analgesia means were 11.5±3.3 minutes in epidural group ,5.2±1 minutes in spinal group ,and 2.7±0.7 minutes in remifentanil group.

Table 2*: Pain intensities (NRS) in different groups (Mean ±SD) + (range).*

Stage of labor	**Epidural group**	**Spinal group**	**Remifentanil group**	**P-value**
First stage before intervention	8.9±1.3 (5-10)	9.4±0.9 (6-10)	8.8±1.8 (3-10)	**0.278**
First stage after intervention	1.8±1.5 (0-7)	3.9±1 (1-6)	4.9±1 (3-7)	**0.01**
Second stage after intervention	3.5±1 (1-5)	2±1 (0-5)	6±1 (5-9)	**0.01**

The complication are presented in table-3, where the remifentanil group showed complications like, SPO2 < 92 % in 20/25 parturients (80%), decrease of respiratory rate below 12 breath/minutes in 4/25 (16%) and Ramsay sedation score was 4, in 5/25 (20%) were significantly higher in this group than the others. There were intravascular complications 3/25 (12%) and intraoperative discomfort 8/25 (32%) in the epidural group higher than the other groups. There were no inter- group significant differences in hypotension, pruritus, rate of cesarean section and fetal outcome. One parturient in spinal group developed fetal bradycardia ended with urgent cesarean section. No parturient had vomiting during the study.

Table 3: *Complications in different groups*

Complications	**Epidural group(n=25)**	**Spinal group(n=25)**	**Remifentanil group(n=25)**	**P-value**
Intravascular complications	3 (12%)	0 (0%)	0 (0%)	**0.044**
Hypotension (Systolic blood pressure <90 mmHg)	8 (32%)	3 (12%)	5 (20%)	**0.228**

SPO_2< 92% without nasal O_2	0 (0%)	0 (0%)	20 (80%)	**0.001**
respiratory rate below 12 breath/min	0 (0%)	0 (0%)	4 (16%)	**0.014**
Pruritus	1 (4%)	4 (16%)	0 (0%)	**0.062**
Vomiting	0 (0%)	0 (0%)	0 (0%)	**-------**
Ramsay Sedation score= 4	0 (0%)	0 (0%)	5 (20%)	**0.001**
Intraoperative discomfort during intervention	8 (32%)	5 (20%)	2 (8%)	**0.069**
Cesarean section rate	3 (12%)	3 (12%)	1 (4%)	**0.543**

All parturient received supplements intravenous fluids in both epidural and spinal groups, and five parturients in remifentanil group. All parturients in remifentanil group received continuous oxygen by nasal cannula, one parturient in spinal group and no one in epidural group. Only one parturient in epidural group received IV ephedrine as seen in table-4.

Table 4: *Management during intervention*

Management	Epidural group	Spinal group	Remifentanil group	P-value
Parturients received IV Fluid	25 (100%)	25 (100%)	5 (20%)	**0.001**
Parturients received oxygen	0 (0%)	1 (4%)	25 (100%)	**0.001**
Parturients received IV ephedrine	1 (4%)	0 (0%)	0 (0%)	**0.373**

The second stage duration was more in epidural group than in spinal and remifentanil groups and there was a significant difference between epidural and remifentanil groups, (P= 0.031) as in table-5.

Table 5: *Second stage duration in minutes*

Group	Means	Mean difference	P-value
Epidural-spinal	19.4-16.8	2.5	0.563
Epidural-remifentanil	19.4-9.5	9.5	0.031
Spinal-remifentanil	16.8-9.5	7	0.111

Maternal satisfaction was higher in both epidural and spinal groups, and there is a significant difference between epidural and remifentanil groups (P=0.032) as in table-6.

Table 6: *Maternal satisfaction*

Group	Score means	Mean difference	P-value
Epidural-spinal	2.8-2.8	0.04	**0.756**
Epidural-remifentanil	2.8-2.5	0.28	**0.032**
Spinal-remifentanil	2.8-2.5	0.24	**0.065**

There were no significant differences between the neonatal outcomes in the three groups in Apgar score measured at the first and five minutes.

5 | DISCUSSION

The chief role of the anesthesiologist is to provide safe labor analgesia (15). In this study we used three pharmacological regimens for pain relief during labor with different routes of administration: epidural, intrathecal and intravenous. The aim is to compare the efficacy, complications and maternal satisfaction between the standard method the epidural with the intrathecal and the intravenous remifentanil analgesia during labor to find alternative to the epidural analgesia. All women in

the epidural group demonstrated a significant decrease in pain scores in the first stage of labor compared with the spinal and remifentanil groups (P<0.05),this goes with the recommendations of the ASA and the ACOG (10). Intrathecal fentanyl has become popular for labor analgesia in recent years; at a dose of 25 µg (20). Fentanyl provides analgesia of relatively rapid onset with a mean duration of approximately 90 minutes (21). Side effects are usually easily managed, and there is no associated motor block (31). In an effort to improve analgesia and duration, bupivacaine had been used by Collis et al as an adjunct to intrathecal fentanyl for labor (31). Findings indicate that adding hyperbaric bupivacaine 2.5 mg to intrathecal fentanyl 25µg significantly prolongs the duration of effective analgesia, and hastened the onset (17, 19). Although intrathecal opioids should have no effect on motor pathways or muscle strength, local anesthetic can cause motor block. However collis et al reported that this combination (fentanyl 25µg and bupivacaine 2.5 mg) intrathecally had little effect on motor pathways and all parturient where able to perform a straight leg raise against resistance and our results were the same. By using this intrathecal combination our results indicated that was not effective as the epidural in relieving labor pain in the first stage, while it was higher effective than epidural in relieving labor pain in the second stage and there was a significant difference (P<0.05). However the maternal satisfaction was similar in both groups with no significant difference. The possibility that intrathecal fentanyl might be associated with fetal heart-rate abnormalities due to uterine hyperactivity was initially raised by Clarke et al (32). Subsequently, Collis et al (31) noted no difference between intrathecal fentanyl and standard epidural groups in the rate of fetal bradycardia after injection. Palmer et al (33) compared intrathecal fentanyl and standard epidural techniques for labor and found no difference between the two groups in the incidence of fetal heart-rate abnormality, and no effect on need for urgent delivery or ultimate delivery route, while in our study one parturient developed fetal bradycardia and needed urgent cesarian section. We chose the same dose of remifentanil which Volmanen et al (34) showed as an effective dose without desaturation in labor. In addition, there is evidence suggesting that continuous infusions may produce less sedation than larger intermittent boluses (35). In the present study a calculated weight-based dose was administered, however in other studies, an average dose of drug was administered rather than a calculated weight-based one (36, 37). Ideally it is better to administer the dose as necessary with progression of labor, especially as acute tolerance can develop with prolonged use of remifentanil (38).Maternal safety is a concern with any opioid-based analgesic technique including remifentanil during labor. Sedation scores increased over the time in this study. However, these increases in sedation were usually from “awake” to “drowsy” and most women (80%) remained “responsive to voice (Ramsay score grade 3)” throughout. The short duration of action and lack of accumulation of remifentanil imply that any problems with sedation would be quickly reversed (37). Our study confirmed that utilizing nasal oxygen, episodes of desaturation did not occur. However Blair et al reported some episodes of desaturation in remifentanil usage, although the majority of them also used Entonox throughout the study period and this may have contributed to that respiratory depression (37) .In our study the Apgar score was similar in all groups and the averages of fetal heart rates were in the normal range (120-140). The study was completed without obvious clinical side effects for infants. Investigation of remifentanil pharmacokinetics in infants under 2 months provided an explanation of why the fetus is relatively unaffected by exposure to remifentanil: its half-life in this population was found to be equal to that in adults (39). However, fetus is able to metabolize remifentanil crossing the placenta rapidly. Three previous trials investigated the efficacy of a remifentanil PCA (51 patients) in comparison with an epidural catheter (51 patients) (30, 39, 40). In all trials, women in the remifentanil group had a higher mean pain score after 1 hour in comparison with the epidural group there were no significant differences in the incidence of spontaneous delivery, instrumental delivery or

cesarean section. Satisfaction scores with the analgesic regimens were comparable (30, 40). In all trials, patients receiving remifentanil showed a greater risk of oxygen desaturation (RR 16.04, 95%CI 3.33–77.32, P<0.001, I2¼0%). There were no significant differences in cardiotocography tracings recorded in all group, (30, 39, 41). In the present study the results were the same and comparable with these trials and indicated that intravenous remifentanil during labor and delivery was associated with a minimal decrease in pain score, acceptable sedation score and maternal respiratory complication were significantly more in remifentanil group compared to epidural and spinal groups, so oxygen supply by nasal route was necessary. However maternal satisfactions were not comparable and were lowest in the remifentanil group. Our findings of an absence of any fetal or neonatal adverse effects are consistent with other studies (41, 42, 43, 44). Other findings are in contradictory (45, 46, 47) with respect to maternal and neonatal side effects, which can be explained by the various doses used and mode of administrations. The concomitant use of a background infusion is controversial (48), some studies recommended the use of a background infusion (41), and others argued that remifentanil administration without a background provides safe but incomplete analgesia (50). Because of the fact that it is difficult, to coincide the peak effect of remifentanil with each uterine contraction (51) , a background infusion was chosen in this study to provide constant baseline analgesia and that only the contraction peaks required rescue boluses. In our study we did not use the patient controlled analgesia (PCA) for intravenous remifentanil infusion because it was not available in our hospital at that time. While most previous studies used PCA for controlling intravenous remifentanil infusion according to the parturient need. The result of our study were not satisfied comparing with others in which the results indicate that the use of PCA intravenous remifentanil for parturient during labor and delivery is associated with a decrease in Visual Analog pain Score (VAS), acceptable sedation score, and good patient satisfaction that is comparable to the epidural techniques. This is almost when use the PCA for intravenous remifentanil, the patient will benefits from a greater sense of controlling her pain management, plus the anxiolytic effect of using narcotic (remifentanil), which is an important psychological effect that contributes to the success of this technique (51).

6 |CONCLUSION

The most effective analgesia during the first stage of labor was the epidural, while in the second stage was the spinal analgesia. While Maternal respiratory complications were significantly more in the remifentanil group. Maternal satisfaction was higher in both epidural and spinal than the intravenous remifentanil.

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